

II. "Photographic Determination of the Time-relations of the Changes which take place in Muscle during the Period of so-called 'Latent Stimulation.'" By J. BURDON SANDERSON, F.R.S. Received April 17, 1890.

It is now forty years since Helmholtz published his fundamental experiments on the time-relations of muscular contractions. The purpose of this investigation was to ascertain "the periods and stages in which the energy of muscle rises and sinks after instantaneous stimulation;" the word energy being defined as the "mechanical expression of activity;" and one of the most important conclusions of the author was that, in the muscles investigated by him, contraction does not begin until nearly one hundredth of a second after excitation. This interval has, by subsequent writers, been called the period of "latent stimulation."

Helmholtz subsequently (1854) showed, by experiments of surpassing ingenuity, that during this period an electrical change of very short duration occurs, which culminates at about one two-hundredth of a second after excitation. The fact discovered by Helmholtz was further investigated by Bernstein in 1866, with the aid of the repeating rheotome, and subsequently (1875) by du Bois-Reymond, whose statement of the actual time-relations of the electrical response to an instantaneous excitation of the gastrocnemius of the frog is embodied in a curve which denotes that the muscular surface becomes negative to the tendon about three thousandths of a second after excitation, that this effect culminates at seven thousandths of a second, and that it is immediately followed by a change of opposite sign, which culminates at about ten thousandths.

The statement enunciated above may be taken to represent the present state of knowledge on the subject of the "negative variation" or electrical response of muscle to an instantaneous stimulus; but, as regards the mechanical response, a great effort has been made of late years to obtain a more accurate measurement of the period of latent stimulation by methods founded on those originally employed by Helmholtz, with the result that it has been shortened very considerably. Two observers, viz., Professor Tigerstedt, of Stockholm, and more recently Professor Yeo, F.R.S., have, by improved methods, obtained records from which they conclude that the duration of the period is 0.005". Finally, Professor Regecsky, of Pesth, has, by avoiding certain sources of error, obtained curves which lead him to conclude that the mechanical response may begin "at the moment of direct excitation"—in other words, that the period of latent stimulation does not exist.

I have now to submit to you incontrovertible evidence which the photographic method affords, not only that the estimate of the duration of the period of latent stimulation accepted as true ever since Helmholtz's early investigations is very much too long; but that the final conclusion arrived at by Dr. Yeo a year ago, that it has a real duration of five thousandths of a second, is erroneous. I am further in a position to demonstrate what are the time-relations of the electrical change to the muscular contraction with which it is associated.

The method of observation consists in projecting the movement to be recorded, whether of the muscle or that of any instrument which serves as an index of change, on a vertical slit on which the vibrations of a tuning-fork and the motion of a signal are also shadowed. Immediately behind the slit is a photographic plate, which is carried by an equilibrated pendulum. The approximately uniform rate of motion of the sensitive surface which receives the light-written record is about one meter per second, but is determined in each experiment by reference to the rate of vibration of a tuning-fork.

The plan adopted for obtaining a photographic record of the earliest trace of change of form, was based on the by no means new consideration that the effect of an instantaneous stimulus is in the first instance limited to the part of the structure to which it is applied, and, consequently, may fail to produce any measurable change of form of the whole muscle; the parts which first contract doing so at the expense of the as yet relaxed parts which are connected with them. This consideration is applicable not only to the case in which the muscle is excited directly, but also to that in which it is excited through its nerve; for in the latter case, each fibre is first stimulated at the spot at which it receives its nerve.

In the experiments on direct excitation, the muscles used were the *gastrocnemius* and *sartorius* of the frog. In the former the movement of contraction was communicated to a light index, which was supported by a fine spring. One end of the index rested on the muscle, while the other occupied the front focus of a projection apparatus, the slit being in the other focus. When the *sartorius* was used the surface of the muscle was itself brought for a moment into the focus, at the seat of excitation. The unavoidable exposure of the structure to the electric light, which this method involved, lasted scarcely more than a second. In successful experiments, the interval between excitation and the beginning of the contraction was $2\frac{1}{2}$ thousandths ($= \frac{1}{400}$) of a second.

In a photographic record of a succession of events no time-error is possible, provided that the rate of movement of the recording surface remains unaltered, for, if I may so express myself, an event cannot be seen photographically before it happens. It is therefore certain

that, in direct excitation, contraction begins not more than one four-hundredth of a second after an instantaneous stimulus.

For measurement of the delay in indirect excitation, the gastrocnemius (with the index) only was used, the exciting electrodes being applied either at 12 or at 37 mm. from the muscle. The results were not so constant. Corrected for loss of time by propagation along the nerve, the intervals between excitation and beginning contraction varied from 0.0025'' to 0.0035''.

In the experiments for determining the time after excitation at which the electrical response begins and culminates, the capillary electrometer was used, as in my experiments on the heart and on the leaf of *Dionæa*, as a signal, but with much improved apparatus for recording.

In the gastrocnemius of the frog, the electrical response to an instantaneous stimulus is indicated by a sudden movement of the mercurial column of so short a duration, that to most persons it is invisible. Its photographic expression is that of a spike projecting from the dark border of the part of the plate which is unprotected by the mercurial column. The electrical interpretation of this spike is that between the contacts two electrical changes of opposite sign and not more than one two-hundredth of a second in duration have immediately followed each other, or, more explicitly, that the spot excited became, for about 0.0005'', first negative, then for a similar period positive, to the other contact (see last paragraph).

Before using the electrometer as a signal it was necessary to ascertain that, under the conditions of the experiment, there was no delay in the circuit, either due to sluggishness of the instrument or to any other cause. It was proved photographically that there is no measurable delay.

In the muscle (the leading off contacts being on the Achilles tendon and muscular surface respectively, and the nerve excited at a distance of 12 mm.) the electrical response begins at 0.004'', and culminates at about 0.012'' after excitation. Deducting the delay due to transmission along the nerve, we have, as the time between excitation and response, 0.0035''. It is thus seen that the electrical response, instead of preceding the mechanical, is contemporary with it. All those theories therefore of the excitatory process in muscle which rest on the supposed fact that electrical disturbance is a concomitant of the period of latent stimulation, fall to the ground. The electrical change *may*, so far as concerns the time at which it occurs in muscle, be immediately connected with that sudden change of the elastic properties of muscle of which the contraction is the sign.

The fact that there is a measurable interval of time between excitation and electrical response, renders it improbable that Regecsky is right in supposing that the contraction begins at the moment of

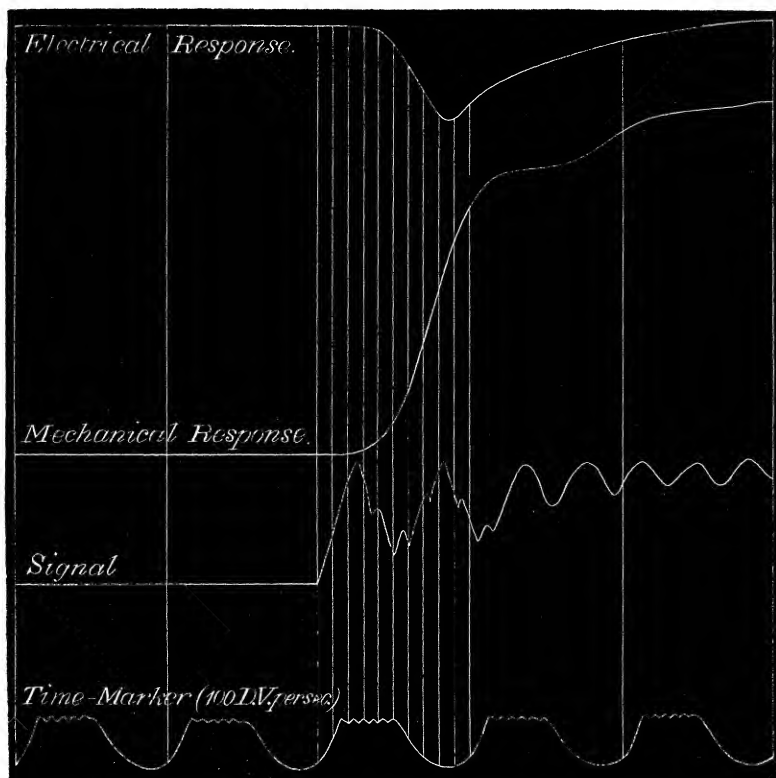


Diagram showing the time-relations of the electrical response (relative negativity succeeded by relative positivity of the longitudinal surface of the gastrocnemius, excited indirectly), and of the mechanical response (beginning of contraction of the same muscle excited directly).

The horizontal distance of the closer vertical lines from each other corresponds to $\frac{1}{1000}$ of a second. The photographic curves were copied twice their natural size by "projecting" them on a sheet of paper.

stimulation. It can scarcely be imagined that the electrical change is later than the mechanical.

The statement above as to the interpretation of the photographic record of the electrical response is founded on the following experimental facts. When a current of very short duration is led through the electrometer, of such strength as to produce a movement of the mercurial column comparable with those observed in the experiments above described, the photographic record shows first that the mercurial column during the passage of the current executes a rapid movement

in the same direction, and that at the cessation of the current the meniscus does not return, or returns very slowly, describing on the photographic plate a curve, of which the characters will be discussed in a paper to be shortly submitted to the Society by Mr. Burch. It is sufficient to say that the reason why the meniscus returns so slowly is that the potential of the charge which it has received is proportional to the displacement; in the case of a current of very short duration it is inconsiderable as compared with the difference of potential of the terminals at the moment that the current is broken.

When, instead of a single current in one direction (one two-hundredth second), two currents of the same duration follow each other in opposite direction, the record resembles in its essential characters that of the excitatory electrical response in muscle. It is seen that the mercurial column, which is displaced during the brief duration of the first current, returns abruptly to the previous position during the second. These phenomena I leave also to be discussed subsequently, noting only that the difference of potential at the terminals of the electrometer which is required to bring back the column to its original position is the same as that by which it was displaced, and that such an effect as has been described in muscle could not be produced by the becoming negative of the middle of each muscular fibre, unless that change were followed either by another in the opposite direction at the seat of excitation, or by a similar change at the other electrode.

Considering that the known velocity of propagation of the excitatory process in the muscle of the frog is about 3 meters, and that the distance between the contacts is about 1.5 cm., we should expect that if the two currents through the electrometer, the existence of which the photographic record so distinctly indicates, were due to propagation, they should follow each other at an interval of one two-hundredth of a second. The actual difference of time between the two electrical effects lies fairly within this estimate.

Postscript, April 28th.—Since sending this communication, I have become aware of a research published very recently by Professor Bernstein ("Ueber den mit einer Muskelzuckung verbundenen Schall und das Verhältniss desselben zur negativen Schwankung."—"Untersuch. aus dem Physiol. Institut der Universität Halle," 1890), which relates closely to the subject of this paper. The facts observed, though of a different order from those recorded above, afford a remarkable confirmation of them. They are as follows:—When a muscle (gastrocnemius of a rabbit) is excited by a single induction current applied to its nerves, its tendon and muscular surfaces respectively being connected with a telephone, the electrical response can be heard telephonically. This Bernstein calls the electrical thud (*electrischer Stoss*). A thud of a similar character may be heard by

auscultation. If telephone and stethoscope are applied to the same ear, one sound only is heard. Exner has shown that any two sounds which are as much as $\frac{1}{500}$ of a second apart are audible as distinct sounds. Bernstein therefore concludes that, inasmuch as contraction begins nearly $\frac{1}{100}$ second after excitation, and the electrical change culminates at $\frac{1}{200}$ second, the mechanical thud must, as well as the electrical, be molecular, and concludes that the two sounds are coincident. In the second of these conclusions, Professor Bernstein appears to be justified, but not in the first. It having been shown by the photographic records that the two responses, the electrical and the mechanical, are nearly coincident, it is no longer needful to seek an explanation of the fact that the electrical and mechanical sounds are indistinguishable.

III. "The Development of the Sympathetic Nervous System in Mammals." By A. M. PATERSON, M.D. Communicated by A. MILNES MARSHALL, F.R.S. Received April 18, 1890.

(Abstract.)

The following investigations were undertaken with the object of determining the origin of the Mammalian sympathetic system, and of clearing up thereby certain points in its morphology.

Two opposite views exist at present among embryologists regarding its development. In both views the segmental formation of the sympathetic cord is upheld. According to the older view (Remak, &c.), it is mesodermal, and is formed *in situ*. According to more recent views, it is ectodermal. Balfour and Onodi, who have maintained the latter view, differ, however, as to the fundamental origin of the sympathetic system,—Balfour regarding each sympathetic ganglion as an offshoot from the spinal nerve, while Onodi considers it a direct proliferation from the spinal ganglion.

For the present research mammalian embryos were exclusively employed—rat, mouse, rabbit, and human embryos. The stage in development was first considered in which the sympathetic system was plainly visible, and from this point the earlier and later stages in the process were traced. It was only possible to determine approximately the ages of the embryos employed, as the time of impregnation varies in different instances, and two embryos from the same uterus often differ in size and extent of development.

The first event to occur is the formation of the main sympathetic cord. In very young embryos (*e.g.*, rabbit, 7 days, axial length 5 mm.), in which the spinal nerves are completely formed and the spinal ganglia clear and distinct, there is no trace of the sympathetic

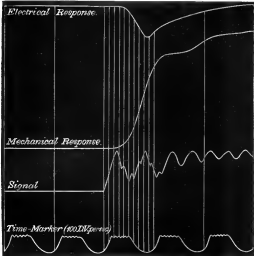


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